

### **Remarks**

Claims 4-5 and 37-56 are pending. Claims 37-56 are allowed.

In response to the Office Action dated April 4, 2002, each one of the cited references has been reviewed, and the rejections and objections made to the claims by the Examiner have been considered. Applicants have traversed all rejections and objections regarding all pending claims, and therefore allowance of these claims is earnestly solicited.

### **Rejections under 35 USC §112, second paragraph**

The Examiner rejects claims 4-5 under 35 USC §112, second paragraph as being indefinite. More specifically, the Examiner states that the phrase "titer of HT1080 cells" is vague. Pursuant to the Examiner's suggestion, claims 4-5 have been amended to recite "a titer of viruses on HT1080." Accordingly, Applicants submit that the claims as presented in the amendment conform to all applicable requirements under 35 USC §112 and respectfully request that the rejections be withdrawn. Applicants note that such amendments are not intended to limit the claimed invention. Rather, such amendments are made solely in response to the Examiner's rejections.

### **Rejections under 35 USC §103**

The Examiner rejected claim 4 as being unpatentable over Pensiero in view of Mulligan and Hermann. The Examiner states that the present invention is essentially taught by Pensiero, and the secondary references, Mulligan and Hermann, merely recite that human factor VIII gene and method for maintaining high titers of retroviral vectors, respectively. The Examiner concludes that a person of ordinary skill in the art would have been motivated to combine Pensiero with Mulligan in order to generate recombinant replication defective retroviral vectors which are resistant to inactivation by human complement and which

express human factor VIII and to utilize the teachings of Hermann on storage of retroviral vectors to maintain high titers of the retrovirus.

In response, the Applicants submit that the Examiner has not established a *prima facie* case of obviousness because the Examiner has not established that August 17, 1994 is a valid 102(e) date for U.S. Patent 6,329,199. According to MPEP §2136.03 (IV), the filing date of U.S. Parent application can only be used as the 35 USC §102(e) date if it supports the claims of the issued child. The issued Pensiero patent, USPN 6,329,199, is a child of a string of abandoned applications that were continuation-in-parts. The Examiner has not established that the parent application 08/291,765 filed August 17, 1994 supports the claims of the 6,329,199 patent as required by 35 USC §112, first paragraph. "For if a patent could not theoretically have issued the day the application was filed, it is not entitled to be used against another as 'secret prior art'" under 35 USC §102(e). *In re Wertheim*, 646 F.2d 527, 537, 209 USPQ 554, 564 (CCPA 1981).

Assuming, arguendo, that the August 17, 1994 application discloses and supports the subject matter of Pensiero (USPN 6,329,199), the Applicant respectfully submits that the Examiner has impermissibly used hindsight to render the present invention obvious. Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight. *In re Dembiczak*, 175 F.3d 994, 999 (CAFC 1999). The *In re Dembiczak* court further states:

"evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem solved, although 'the suggestion more often comes from the teachings of the pertinent references,' *In re Rouffet*, 149 F.3d 1350, 1355 (Fed. Cir. 1998). The range of sources available, however, does not diminish the requirement for actual evidence. *That is, the showing must be clear and particular.* See, e.g., *C.R. Bard*, 157 F.3d 1340, 1352, 48 USPQ2d. 1225,

1232 (F. d. Cir. 1998). *Broad conclusory statements regarding the teachings of multiple references, standing alone, are not 'evidence'* (emphasis added). *In re Dembiczak*, 175 F.3d at 999.

After detailed analysis of the cited prior art references, it is not apparent to the Applicants that there is clear and particular objective evidence or teachings that would motivate a person of ordinary skill to combine these prior art references. For instance, Pensiero teaches that retroviruses that are resistant to lysis by human serum, but it does not disclose high titers of the retrovirus. However, Applicants respectfully submit that it is not apparent from the teachings of Hermann to suggest or motivate a person of ordinary skill in the art to provide a high titer preparation as recited in claim 4. That is, Hermann merely discloses methods of preserving recombinant retroviruses that may have a titer of  $10^6$  cfu/ml. No where does Hermann teach or suggest a preparation of replication defective retroviruses wherein the vector preparation has a titer on HT1080 cells or greater than  $10^6$  cfu/ml. In the absence of teachings to perform greater than  $10^6$  cfu/ml titers on HT1080 cells, the Applicants assert that the more efficient HT1080 cell line as recited in the present invention would not have been obvious to one of ordinary skill in the art. Furthermore, combining the teachings of Pensiero, Mulligan, and Hermann to arrive at the present invention would require considerable modification and the exercise of inventive skill by a person of ordinary skill in the art. Accordingly, Applicants respectfully submit that the rejection to claim 4 has been traversed and allowance of claim 4 is earnestly solicited.

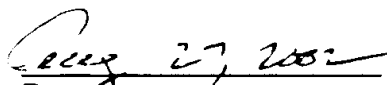
### CONCLUSION

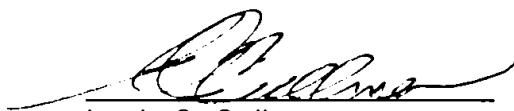
Claims 4-5 and 37-56 are currently pending. Claims 4-5 and 37-56 are allowed. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version With Markings to Show Changes Made."

If for any reason direct communication with Applicants' attorney would serve to advance prosecution of this case to finality, the Examiner is cordially urged to call the undersigned attorney at the below listed telephone number.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-1901.

Respectfully submitted,

  
Date

  
Louis C. Cullman  
Registration No. 39,645

OPPENHEIMER WOLFF & DONNELLY, LLP  
840 Newport Center Drive, Suite 700  
Newport Beach, CA 92660  
Telephone: 949.823.6000  
Facsimile: 949.823.6100

**VERSION WITH MARKINGS SHOWING CHANGES MADE**

Please amend claims 4-5 as follows:

4. (Twice Amended) A preparation of replication defective recombinant retrovirus expressing human factor VIII protein, wherein said recombinant retrovirus is capable of infecting human cells and is resistant to degradation by human complement, wherein said recombinant retrovirus preparation has a titer of HT1080 cells [of] on greater than  $10^6$  cfu/ml.

5. (Twice Amended) A preparation of replication defective recombinant retrovirus expressing human factor VIII protein, wherein said recombinant retrovirus is capable of infecting human cells and is resistant to degradation by human complement, wherein said retrovirus preparation has a titer of HT1080 cells [of] on greater than  $10^7$  cfu/ml.